

CLAIMS

1. A composition for preparing a stimuli responsive hybrid hydrogel comprising a polymeric network consisting essentially of a water soluble polymer crosslinked by a protein domain.

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2. A composition according to Claim 1 wherein the crosslinking of the protein domain to the polymer is by means of non-covalent bonding selected from the group consisting of chelation bonding, coordination bonding, biotin-^{avidin} bonding, protein-protein interaction and protein-ligand interaction.

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3. A composition according to Claim 2 wherein the crosslinking of the protein domain to the polymer is by means of chelation bonding.

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4. A composition according to Claim 2 wherein the crosslinking of the protein domain to the polymer is by means of biotin-^{avidin} bonding.

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5. A composition according to Claim 2 wherein the crosslinking
of the protein domain to the polymer is by means of protein-
protein interaction.

5 6. A composition according to Claim 2 wherein the crosslinking
of the protein domain to the polymer is by means of protein-
ligand interaction.

7. A composition according to Claim 1 wherein the crosslinking
of the protein domain to the polymer is by means of covalent or
coordination bonding.

8. A composition according to either Claims 2 or 7 wherein the
protein domain has a coiled-coil structure.

15 9. A composition according to either Claims 2 or 7 wherein the
protein domain is a recombinant protein domain.

10. A composition according to either Claims 2 or 7 wherein the
20 water soluble polymer is a member selected from the group
consisting of copolymers of N-substituted methacrylamides,

copolymers of N, N-disubstituted acrylamides, hydrophilic esters
of methacrylic or acrylic acid, N-vinylpyrrolidone, N-
acryloylmorpholine, sulfoethylmethacrylate, acrylic and
methacrylic acid, di-block copolymers of polyethylene oxide (PEO)
5 and polypropylene oxide (PPO), and tri-block copolymers of
polyethylene oxide (PEO) and polypropylene oxide (PPO) and the
derivatives thereof.

11. A composition according to Claim 10 wherein the water soluble
10 polymer is *a Copolymer of* ~~an~~ N-substituted methacrylamide and the derivatives
thereof.

12. A composition according to Claim 11 wherein the N-
substituted methacrylamide is a member selected from the group
15 consisting of N-(2-hydroxypropyl)methacrylamide (HPMA),
copolymers of N-(N',N'-dicarboxymethylaminopropyl) methacrylamide
(DAMA), and copolymers of HPMA and N-(3-
aminopropyl)methacrylamide and the derivatives thereof.

13. A composition according to Claim 10 wherein the
water soluble polymer is a member selected from the group
consisting of di-block copolymers of polyethylene oxide (PEO)
and polypropylene oxide (PPO), tri-block copolymers of
5 polyethylene oxide (PEO) and polypropylene oxide (PPO) and the
derivatives thereof.

14. A composition according to Claim 10 wherein the
water soluble polymer is copolymer of a member selected from the
10 group consisting *N-disubstituted* ~~N-disubstituted~~ acrylamides, hydrophilic
esters of methacrylic or acrylic acid, N-vinylpyrrolidone, N-
acryloylmorpholine, sulfoethylmethacrylate, acrylic and
methacrylic acid and the derivatives thereof.

15. A composition according to either Claim 2 or 7 wherein the
molar ratio of the water soluble polymer to the crosslinking
protein domain is within a range of about 1:1 and 1:500.

16. A composition according to Claim 15 wherein the
20 molar ratio of the water soluble polymer to the crosslinking
protein domain is within a range of about 1:1 to 1:300.

17. A composition according to either 2 or 7 further comprising a bioactive agent.

18. A composition according to 17 wherein the bioactive agent is
5 an oligo- or poly-peptide.

19. A composition according to 18 wherein the peptide is conjugated with the crosslinking protein domain.

10 20. A composition according to 17 wherein the bioactive agent is DNA or RNA.

15 21. A stimuli responsive hydrogel comprising the composition of claim 1 in a three dimensional aqueous solution ^{swollen} ~~swelled~~ state.

20 22. A stimuli responsive hydrogel according to Claim 21 wherein the crosslinking of the protein domain to the polymer is by means of non-covalent bonding selected from the group consisting of chelation bonding, coordination bonding, biotin ^{avidin} ~~aviding~~ bonding, protein-protein interaction and protein-ligand interaction.

23. A stimuli responsive hydrogel according to Claim 22 wherein
the crosslinking of the protein domain to the polymer is by means
of chelation bonding.

5 24. A stimuli responsive hydrogel according to Claim 22 wherein
the crosslinking of the protein domain to the polymer is by means
a of biotin-^{avidin} bonding.

10 25. A stimuli responsive hydrogel according to Claim 22 wherein
the crosslinking of the protein domain to the polymer is by means
of protein-protein interaction.

15 26. A stimuli responsive hydrogel according to Claim 22 wherein
the crosslinking of the protein domain to the polymer is by means
of protein-ligand interaction.

20 27. A stimuli responsive hydrogel according to Claim 21 wherein
the crosslinking of the protein domain to the polymer is by means
of covalent or coordination bonding.

28. A stimuli responsive hydrogel according to either Claims 21 or 27 wherein the protein domain has a coiled-coil structure.

29. A stimuli responsive hydrogel according to either Claims 21 or 27 wherein the protein domain is a recombinant protein domain.

30. A stimuli responsive hydrogel according to either Claims 21 or 27 wherein the water soluble polymer is a member selected from the group consisting of copolymers of N-substituted
N-disubstituted
methacrylamides, copolymers of *N,N-disubstituted* acrylamides, hydrophilic esters of methacrylic or acrylic acid, N-vinylpyrrolidone, N-acryloylmorpholine, sulfoethylmethacrylate, acrylic and methacrylic acid, di-block copolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO), and tri-block copolymers of polyethylene oxide (PEO) and polypropylene oxide (PPO) and the derivatives thereof.

31. A stimuli responsive hydrogel according to Claim 30 wherein
a Copolymer of
the water soluble polymer is ~~an~~ N-substituted methacrylamide and
the derivatives thereof.

32. A stimuli responsive hydrogel according to Claim 31 wherein
the N-substituted methacrylamide is a member selected from the
group consisting of N-(2-hydroxypropyl) methacrylamide (HPMA),
copolymers of N-(N',N'-dicarboxymethylaminopropyl) methacrylamide
5 (DAMA), and copolymers of HPMA and N-(3-
aminopropyl) methacrylamide and the derivatives thereof.

33. A stimuli responsive hydrogel according to Claim 30 wherein
the water soluble polymer is a member selected from the group
10 consisting of di-block copolymers of polyethylene oxide (PEO)
and polypropylene oxide (PPO), tri-block copolymers of
polyethylene oxide (PEO) and polypropylene oxide (PPO) and the
derivatives thereof.

15 34. A stimuli responsive hydrogel according to Claim 30 wherein
the water soluble polymer is copolymer of a member selected from
the group consisting of ^{N-disubstituted} ~~N,N-disubstituted~~ acrylamides, hydrophilic
esters of methacrylic or acrylic acid, N-vinylpyrrolidone, N-
20 acryloylmorpholine, sulfoethylmethacrylate, acrylic and
methacrylic acid and the derivatives thereof.

35. A stimuli responsive hydrogel according to either Claim 21 or 27 wherein the molar ratio of the water soluble polymer to the crosslinking protein domain is within a range of about 1:1 and 1:500.

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36. A stimuli responsive hydrogel according to Claim 35 wherein the malor ratio of the water soluble polymer to the crosslinking protein domain is within a range of about 1:1 and 1:300.

10 37. A stimuli responsive hydrogel according to either 21 or 27 further comprising a bioactive agent.

15 38. A stimuli responsive hydrogel according to 37 wherein the bioactive agent is a oligo- or poly- peptide.

20 39. A stimuli responsive hydrogel according to 38 wherein the peptide is conjugated the crosslinking protein domain.

40. A stimuli responsive hydrogel according to 37 wherein the
bioactive agent is DNA or RNA molecule.

41. A stimuli responsive hydrogel according to 37 wherein the
bioactive agent is ~~saluted~~^{Soluble} in the aqueous solution.

42. A stimuli responsive hydrogel according to either Claims 21
5 or 27 wherein the aqueous solution in equilibrium swollen state
is with a range of between 1 to 99% (w/w) .

43. A stimuli responsive hydrogel according to either Claims 42
or 27 wherein the aqueous solution in equilibrium swollen state
10 is with a range of between 5 to 99% (w/w) .

44. A stimuli responsive hydrogel according to either Claims 43
or 27 wherein the aqueous solution in equilibrium swollen state
is with a range of between 10 to 99% (w/w) .
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